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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/121,587	07/23/1998	THOMAS J. CHAMBERS	06132/033003	3485

7590 07/02/2002

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EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	34

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/121,587	Applicant(s) CHAMBERS ET AL.	
	Examiner Robert A Zeman	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *3-5,11-13 and 17-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,6-10 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) 1-29 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *29* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 4-24-02 has been entered.

The amendment filed on 4-28-2002 is acknowledged. Claims 3-5, and 11-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Claims 17-29 are withdrawn from consideration as they are drawn to a non-elected invention. Election was made **without** traverse in Paper No. 18. Claims 1,2, 6-10 and 14-16, which read on the elected species, are pending and currently under examination.

Specification

The substitute specification filed 4-28-2002 has not been entered because it does not conform to 37 CFR 1.125(b) because: the substitute specification does not incorporate the changes made by previous amendments.

Objections Maintained

The objection to the specification for the improper use of the trademarks YF-VAX®, JE-VAX® and ChimeriVax™ is maintained for reasons of record since the substitute specification was not entered.

Claim Rejections Withdrawn

The rejection of claims 1, 6-9 and 14-16 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an attenuated chimeric flavivirus comprising of a yellow fever virus whose prM-E coding sequence has been replaced with that of the Japanese Encephalitis virus, does not reasonably provide enablement for an attenuated chimeric flavivirus where the prM-E coding sequences are derived from other flaviviridae (Russian Spring-Summer Encephalitis virus or Omsk Hemorrhagic Fever virus for example) is withdrawn. Applicant's arguments have been demonstrated the specification is enabling for a person skilled in the art to **make** the invention commensurate in scope with these claims.

The rejection of claims 1, 2, 6-10 and 14-16 under 35 U.S.C. 103(a) as being unpatentable over Venugopal et al. (Vaccine 12(11): 966-975, 1994), Rice et al. (The New Biologist: 1(3): 285-296, 1989), Marchevsky et al. (Am. J. Trop. Hyg. 52(1): 75-80, 1995), and Bray et al. (PNAS (USA) 88:10342-10346, 1991) and Chambers et al. (J. Virology 69(3): 1600-1605, March 1995) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive

New Grounds of Rejection

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefore..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v.*

Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1,2, 6-10 and 14-16 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-2, 6-7, 9-11 and 15-18 of copending Application No. 09/452,638. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 and 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic/prophylactic use of the chimeric virus YF/JE SA_{14}-14-2 RMS against Japanese encephalitis virus infection, does not reasonably provide enablement for the therapeutic/prophylactic use of **any other** chimeric flavivirus, nor does it provide enablement for the therapeutic/prophylactic use of YF/JE SA_{14}-14-2 against anything other than Japanese encephalitis virus infection . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification is silent on the efficacy of chimeric viruses (other than YF/JE SA_{14}-14-2) as a therapeutic/prophylactic agent against

flavivirus infections. People of skill in the art require documented factual evidence, that a benefit can be derived by the therapeutic application of a substance. Additionally, to be a prophylactic composition, the composition must elicit protective immunity, demonstrable by viral challenge experiments, in a reasonable model system. The specification, as filed, does not set forth that the claimed composition provides any sort of protective immunity in any model system that can be extrapolated to humans or higher mammals. The instant specification fails to provide direction on what chimeric viruses, other than YF/JE SA_{14}-14-2, are capable of eliciting a therapeutic or a prophylactic response or that a given response would be beneficial to the treated subject. Applicant has failed give direction on what chimeric viruses, other than YF/JE SA_{14}-14-2, would meet the limitations of the claims and has provided no evidence that any benefit to the treated subject would be obtained. Given the lack of success in the art, the lack of working examples, and the unpredictability of the generation of a therapeutic response in a living organism (as illustrated by the increased virulence of the $YF/JE_{Nakayama}$ chimeric virus), the specification, as filed, is not enabling for the use of any other chimeric virus other than YF/JE SA_{14}-14-2 as a therapeutic/prophylactic treatment for flavivirus infection. Nor is it the specification enabling for the use of YF/JE SA_{14}-14-2 as a therapeutic/prophylactic agent against any flavivirus infection other than Japanese Encephalitis virus infection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The claims are drawn to a chimeric, live, infectious, attenuated virus, comprising: a yellow fever virus in which the nucleotide sequence encoding a prM-E protein is modified such that the functional YF virus prM-E protein is not expressed, and integrated into said YF virus a nucleotide sequence encoding a prM-E protein of a second, different flavivirus, specifically the Japanese Encephalitis virus, so that the prM-E protein of said second flavivirus is expressed. The claims are further drawn to the chimeric virus above wherein the nucleotide sequence encoding the prM-E protein of the second flavivirus comprises a mutation that prevents prM cleavage to produce M protein while maintaining the NS2B-3 protease recognition site and signal sequences and cleavage sites at the C/prM and E/NS1 junctions.

Claims 1-2, 6-10 and 14-16 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lai et al. (WO 93/06214 – IDS-22).

Lai et al. disclose an attenuated chimeric flavivirus particle comprising a region of nucleotide sequences encoding the non-structural proteins (NS) of yellow fever virus and a region of nucleotide sequences encoding the structural protein prM-E of a flavivirus selected from a dengue virus (serotype 1, 2, 3 and 4), Japanese encephalitis virus, tick-borne encephalitis virus (specifically) and a flavivirus (generally). Lai et al. specifically disclose the DNA fragment that encodes a dengue virus protein comprising mutations at the C-terminal of the NS1 gene, resulting in the prevention of the NS1 protein cleavage (see examples 8-12). Lai et al. further disclose the use of said chimeric flaviviruses as a vaccine (see example 21) and methods of producing said chimeric viruses recombinantly (see example 17). While Lai et al. do not explicitly disclose methodologies (i.e. provide working examples) using the Yellow Fever virus

and the Japanese encephalitis virus, they disclose "a chimeric virus for use in vaccine preparation having a genome comprising nucleic acid sequences encoding at least one structural protein from one flavivirus and nucleic acid sequences encoding nonstructural proteins from another (see abstract and page 6, lines 18-25) Therefore, while not explicitly disclosed in the working examples, the Yellow Fever/Japanese encephalitis combination would be an obvious variant of the chimeric disclosed in the working examples. One would have had a high expectation of success for, as pointed out by Applicant in Paper No. 32, those of skill in art "could have (and did) design primers for amplification of sequences corresponding to the prM and E regions of other flaviviruses for insertion into the YF two plasmid system" based on the art available at the time of the invention.

Claims 1-2, 6-10 and 14-16 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lai et al. (US Patent 6,184,024 – IDS-29)

Lai et al. disclose an attenuated chimeric flavivirus particle comprising a region of nucleotide sequences encoding the non-structural proteins (NS) of yellow fever virus and a region of nucleotide sequences encoding the structural protein prM-E of a flavivirus selected from a dengue virus (serotype 1, 2, 3 and 4), Japanese encephalitis virus, tick-borne encephalitis virus (specifically) and a flavivirus (generally). Lai et al. specifically disclose the DNA fragment that encodes a dengue virus protein comprising mutations at the C-terminal of the NS1 gene, resulting in the prevention of the NS1 protein cleavage or 3' mutations resulting in reduced glycosylation of prM, E or NS1 resulting in reduced cleavage of the prM protein (see examples

9-16). Lai et al. further disclose the use of said chimeric flaviviruses as a vaccine (see examples 23-24) and methods of producing said chimeric viruses recombinantly (see example 22). While Lai et al. do not explicitly disclose methodologies (i.e. provide working examples) using the Yellow Fever virus and the Japanese encephalitis virus, they disclose "a chimeric virus for use in vaccine preparation having a genome comprising nucleic acid sequences encoding at least one structural protein from one flavivirus and nucleic acid sequences encoding nonstructural proteins from another (see abstract and column 5, lines 58-67 to column 6, lines 1-3). Therefore, while not explicitly disclosed in the working examples, the Yellow Fever/Japanese encephalitis combination would be an obvious variant of the chimeric disclosed in the working examples. One would have had a high expectation of success for, as pointed out by Applicant in Paper No. 32, those of skill in art "could have (and did) design primers for amplification of sequences corresponding to the prM and E regions of other flaviviruses for insertion into the YF two plasmid system" based on the art available at the time of the invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on M-Th 7:30 am - 5:00 pm and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donna Wortman can be reached on (703) 308-1032. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman
July 1, 2002